UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

06/FEB/2007

MEMORANDUM

Subject:	Name of Pesticide Product:	Phyton-016-B
	EPA Reg. No. /File Symbol:	49538-L
	DP Barcode:	D332607
	Decision No.:	370439
	PC Code:	024401

From: Eugenia Mc Andrew, Biologist
Technical Review Branch
Registration Division (7505P)

To: Bryant Crowe, RM Team 22
Fungicide Branch
Registration Division (7505P)

Applicant: Phyton Corporation
7440 West 78th St.
Bloomington, MN 55439

FORMULATION FROM LABEL:

Active Ingredient(s):		% by wt.
024401	Copper Sulphate Pentahydrate*	21.36
Inert Ingredient(s):		78.64
	Total:	100.00%

*Copper as metallic 5.5%

ACTION REQUESTED: The Risk Manager requests review of acute toxicity data for 49538-L.

BACKGROUND: Phyton Corporation has submitted a six pack of acute toxicity studies to support registration of the proposed product, Phyton-016-B, EPA File Symbol 49538-L. The studies were conducted at Product Safety Laboratories, Dayton, New Jersey with assigned MRID numbers 469285-03 to -08. A CSF for a basic formulation dated July 31, 2006 was included in the submission.

RECOMMENDATIONS: The six studies have been reviewed and are classified as acceptable. They do support registration of the proposed product.

The acute toxicity profile for Phyton-016-B, EPA File Symbol 49538-L, is as follows:

Acute oral toxicity	III	Acceptable	MRID 46928503
Acute dermal toxicity	IV	Acceptable	MRID 46928504
Acute inhalation toxicity	IV	Acceptable	MRID 46928505
Primary eye irritation	II	Acceptable	MRID 46928506
Primary skin irritation	IV	Acceptable	MRID 46928507
Dermal sensitization	Neg.	Acceptable	MRID 46928508

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System:

PRODUCT ID #: 049538-00005

PRODUCT NAME: Phyton-016-B

PRECAUTIONARY STATEMENTS

SIGNAL WORD: WARNING

SPANISH SIGNAL WORD: AVISO
Si usted no entiende la etiqueta, busque aque se la explique a usted en detalle.
(If you do not understand the label, find sd someone to read it to you.)

Hazards to Humans and Domestic Animals:

This product meets the criteria for Restricted Use Pesticide due to toxicity categories. It is up to the RM to decide if this product should be classified as Restricted Use. For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification.

Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse. Wear: Long-sleeved shirt and long pants, socks, shoes, and chemical-resistant gloves.

First Aid:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Reviewer: Eugenia McAndrew **Date:** February 6, 2007
Risk Manager: 22

STUDY TYPE: Acute Oral Toxicity - Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid; specific gravity - 1.190 g/mL)

CITATION: Moore, G. Phyton -016-B. Acute Oral Toxicity Study Up and Down Procedure in Rats. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 18394. March 2, 2006. MRID 46928503 Unpublished.

SPONSOR: Phyton Corporation, 7449 Cahill Road, Edina, MN 55439

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46928503), eight female Sprague-Dawley derived young adult albino rats (Age: 9-10 weeks; Source: Ace Animals, Inc., Boyertown, PA; 171-217 g) were given a single oral dose of Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid) using the Up and Down Procedure. A limit dose of 5000 mg/kg of the test substance was administered to one healthy female rat by oral gavage. This animal died so seven additional females were dosed at levels of 175, 550 or 1750 mg/kg. Animals were then observed for up to 14 days after dosing.

Oral LD_{50} Females = 1030 mg/kg (95% C.L. 1750 mg/kg (upper) and 550 mg/kg (lower).

The three females dosed at 175 and 550 mg/kg survived and gained weight. There were no signs of gross toxicity. No gross abnormalities were noted at necropsy. The three females dosed at 1750 mg/kg died within one day of test substance administration. Toxic signs noted prior to death included hypoactivity, hunched posture, piloerection, ano-genital staining and/or diarrhea. Gross necropsy of the decedents revealed discoloration of the intestines. The one animal dosed at 5000 mg/kg died within one hour of test substance administration. Prior to death this animal was hypoactive and exhibited hunched posture. Gross necropsy of the decedent revealed discoloration of the intestines.

Toxicity based on the calculated LD_{50}. EPA Toxicity Category III.

This acute oral study is classified as Acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Individual animals were dosed as follows:

Limit Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	5732	5000	D	D

Main Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	5767	175	S	S
2	5786	550	S	S
3	5845	1750	D	D
4	5867	550	S	S
5	5882	1750	D	D
6	5908	550	S	S
7	5941	1750	D	D

S = survival D = death

A. Mortality - As noted in the table.

B. Clinical observations - The three females dosed at 175 and 550 mg/kg gained weight. There were no signs of gross toxicity. The three females dosed at 1750 mg/kg died within one day of test substance administration. Toxic signs noted prior to death included hypoactivity, hunched posture, piloerection, ano-genital staining and/or diarrhea. The one animal dosed at 5000 mg/kg died within one hour of test substance administration. Prior to death this animal was hypoactive and exhibited hunched posture.

C. Gross Necropsy - No gross abnormalities were noted for the animals dosed at 175 and 550 mg/kg. Discoloration of the intestines was noted in the animals dosed at 1750 and 5000 mg/kg.

D. Reviewer's Conclusions: We agree with the study author that the acute oral LD_{50} of Phyton-016-B is estimated to be 1030 mg/kg of body weight in female rats with an approximate 95% confidence interval of 1750 mg/kg (upper) and 550 mg/kg (lower).

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AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Wednesday, January 31, 2007, 11:28:19 AM
Data file name: .dat
Last modified: 1/31/2007 11:28:19 AM

Test/Substance: Phyton
Test type: Limit Test
Limit dose (mg/kg): 5000
Assumed LD50  (mg/kg): Default
Assumed sigma (mg/kg): 0.5

DATA:

Test  Animal     Dose  Short-term  Long-term
Seq.      ID  (mg/kg)      Result     Result
_____________________________________________
   1    5732     5000           X          X
_____________________________________________
(X = Died, O = Survived)

Dose Recommendation: Stop the limit test and conduct a main test at 175
mg/kg.

SUMMARY OF LONG-TERM RESULTS:

     Dose     O     X     Total
_____________________________________
     5000     0     1         1
_____________________________________
All Doses     0     1         1


AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Wednesday, January 31, 2007, 11:32:43 AM
Data file name: Phyton.dat
Last modified: 1/31/2007 11:32:41 AM

Test/Substance: Phyton
Test type: Main Test
Limit dose (mg/kg): 5000
Assumed LD50  (mg/kg): Default
Assumed sigma (mg/kg): 0.5

Recommended dose progression: 5000, 1750, 550, 175, 55, 17.5, 5.5, 1.75
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DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	5767	175	O	O
2	5786	550	O	O
3	5845	1750	X	X
4	5867	550	O	O
5	5882	1750	X	X
6	5908	550	O	O
7	5941	1750	X	X

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.

Stopping criteria met: 5 reversals in 6 tests.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
175	1	0	1
550	3	0	3
1750	0	3	3
All Doses	4	3	7

Statistical Estimate based on long term outcomes:

Estimated LD50 = 1030 (Based on an assumed sigma of 0.5).
Approximate 95% confidence interval is 550 to 1750.

Reviewer: Eugenia McAndrew **Date:** February 6, 2007
Risk Manager: 22

STUDY TYPE: Acute Dermal Toxicity - Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid)

CITATION: Moore, G. Phyton -016-B. Acute Dermal Toxicity Study in Rats. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 18395. March 2, 2006. MRID 46928504 Unpublished.

SPONSOR: Phyton Corporation, 7449 Cahill Road, Edina, MN 55439

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46928504), two groups of Sprague-Dawley derived young adult albino rats (Age: 9-11 weeks; Source: Ace Animals, Inc., Boyertown, PA; 270-297 g males and 198-240 g females) were dermally exposed to Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid). Five females and five males were exposed to a dose of 5000 mg/kg. Based on the results of this level, five females only were exposed to a dose of 2000 mg/kg. The test substance was applied to a 2 inch x 3 dose area (approximately 10% of the body surface). Test sites were covered with a gauze pad and wrapped with tape for a 24 hour period. After 24 hours the pads were removed. Animals were then observed for 14 days.

Dermal LD_{50} Males > 5000 mg/kg bw
Dermal LD_{50} Females > 5000 mg/kg bw
Dermal LD_{50} Combined > 5000 mg/kg bw

At the 2000 mg/kg dose level (females only), one animal died within four days of test substance administration. Toxic signs noted prior to death included reduced fecal volume, hyperkeratosis and dermal irritation (eschar, edema and erythema). The surviving animals also exhibited hyperkeratosis and dermal irritation (eschar, edema and erythema) at all dose sites. All survivors gained weight. Gross necropsy of the decedent revealed discoloration of the intestines and liver. No gross abnormalities were noted in the survivors. At the 5000 mg/kg dose level (males and females), two females died within three days of exposure to the test substance. Toxic signs noted prior to death included hypoactivity, irregular respiration, reduced fecal volume and dermal irritation (erythema and edema) and hyperkeratosis at the dose site. The surviving animals exhibited dermal irritation (erythema, edema and eschar) and hyperkeratosis at all dose sites from days 1 to 14. The survivors gained weight. Gross necropsy of the decedents revealed discoloration of the intestines and/or lungs. No gross abnormalities were noted for the animals surviving to study termination.

Toxicity based on 2/10 deaths at the limit dose of 5000 mg/kg. EPA Toxicity Category IV.

This acute dermal study is classified Acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
2000	-	1/5	1/5
5000	0/5	2/5	2/10

A. Mortality - As noted in the table

B. Clinical observations - At the 2000 mg/kg dose level (females only), toxic signs noted prior to the one death included reduced fecal volume, hyperkeratosis and dermal irritation (eschar, edema and erythema). The surviving animals also exhibited hyperkeratosis and dermal irritation (eschar, edema and erythema) at all dose sites. All survivors gained weight. At the 5000 mg/kg dose level (males and females), toxic signs noted in the two females prior to death included hypoactivity, irregular respiration, reduced fecal volume and dermal irritation (erythema and edema) and hyperkeratosis at the dose site. The surviving animals exhibited dermal irritation (erythema, edema and eschar) and hyperkeratosis at all dose sites from days 1 to 14. The survivors gained weight.

C. Gross Necropsy - At the 2000 mg/kg dose level, gross necropsy of the decedent revealed discoloration of the intestines and liver. No gross abnormalities were noted in the survivors. At the 5000 mg/kg dose level, gross necropsy of the decedents revealed discoloration of the intestines and/or lungs. No gross abnormalities were noted for the animals surviving to study termination.

D. Reviewer's Conclusions: We agree with the study author that the acute dermal LD_{50} of Phyton-016-B appears to be greater than 5000 mg/kg bw in male and female rats.

Reviewer: Eugenia McAndrew **Date:** February 6, 2007
Risk Manager: 22

STUDY TYPE: Acute Inhalation Toxicity - Rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid)

CITATION: Moore, G. Phyton -016-B. Acute Inhalation Toxicity Study in Rats - Limit Test. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 18396. March 2, 2006. MRID 46928505 Unpublished.

SPONSOR: Phyton Corporation, 7449 Cahill Road, Edina, MN 55439

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 46928505), 5/sex of young adult Sprague-Dawley rats (Age: 9-10 weeks; Source: Ace Animals, Inc., Boyertown, PA; 279-309 g males and 205-229 g females) were exposed whole body via the inhalation route to Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid) for 4 hours at a concentration of 2.06 mg/L. Animals were then observed for 14 days.

LC_{50} Males > 2.06 mg/L
LC_{50} Females > 2.06 mg/L
LC_{50} Combined > 2.06 mg/L

All animals survived and gained weight. Hunched posture and hypoactivity were noted during the exposure period. Following exposure, 5/10 animals exhibited red ocular discharge. The animals recovered from these symptoms by day 3. No gross abnormalities were noted at necropsy. The gravimetric chamber concentration was 2.06 mg/L and the mass median aerodynamic diameter was estimated to be 3.5 µm with a geometric standard deviation of 2.21.

Toxicity is based on no deaths at the limit dose. EPA Toxicity Category IV.

This acute inhalation study is classified as Acceptable. It does satisfy the guideline requirement for an acute inhalation study (OPPTS 870.1300; OECD 403) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Nominal Conc. (mg/L)	Gravimetric Conc. (mg/L)	MMAD µm	GSD	Mortality/Number Tested		
				Males	Females	Combined
76.50	2.06	3.5	2.21	0/5	0/5	0/10

Test Atmosphere / Chamber Description:

Chamber Volume:	150 L
Airflow:	50.9 LPM
Temperature:	21-23°C
Relative Humidity:	45-72%
Time to Equilibrium T_{99}:	13.6 min.

Test atmosphere concentration - Gravimetric samples were withdrawn at 6 intervals from the breathing zone of the animals. Filter papers were weighed before and after collection to determine the chamber concentration. This value was divided by the total volume of air sampled to determine the chamber concentration.

Particle size determination - Particle size was determined twice during the exposure. The MMAD and geometric standard deviation were determined graphically using the two-cycle logarithmic probit axes.

A. Mortality - None

B. Clinical observations - All animals gained weight. Hunched posture and hypoactivity were noted during the exposure period. Following exposure, 5/10 animals exhibited red ocular discharge. The animals recovered from these symptoms by day 3.

C. Gross Necropsy - No gross abnormalities were noted.

D. Reviewer's Conclusions: We agree with the study author that the acute inhalation LC_{50} of Phyton-016-B is greater than 2.06 mg/L in male and female rats.

Reviewer: Eugenia McAndrew **Date:** February 6, 2007
Risk Manager: 22

STUDY TYPE: Primary Eye Irritation - Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid; pH 4.5)

CITATION: Durando, J. Phyton -016-B. Primary Eye Irritation Study in Rabbits. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 18079. October 4, 2005. MRID 46928506 Unpublished.

SPONSOR: Phyton Corporation, 7449 Cahill Road, Edina, MN 55439

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46928506), Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid) was instilled into the conjunctival sac of the right eye of three young adult New Zealand albino rabbits (1 male and 2 females; Source: Robinson Services, Inc., Clemmons, NC). The left eye served as the control. 0.1 mL of the test substance was instilled into the right eye of the first rabbit. Immediately following instillation, the animal exhibited signs of distress. Two drops of ocular anesthetic (Tetracaine Hydrochloride Ophthalmic Solution, 0.5%) were placed into both the treated and control eye of each remaining animal. 0.1 mL of the test substance was then instilled into the right eyes of the next two animals. Animals were observed at 1, 24, 48, 72 hours and at 4, 7, 10 and 14 days post-instillation. Irritation was scored by the method of Draize. Fluorescein dye was used to evaluate the extent of corneal damage or to verify reversal of effects.

All eyes exhibited corneal opacity, iritis and conjunctivitis from the one hour observation through 72 hours. No positive scores were noted for conjunctivitis on day 7. Corneal opacity and iritis resolved by day 14 when all eyes were free of irritation.

In this study, the formulation is moderately irritating to the eye. EPA Toxicity Category II.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

	Number "positive"/number tested							
Observations	**Hours**				**Days**			
	1	**24**	**48**	**72**	**4**	**7**	**10**	**14**
Corneal Opacity	3/3	3/3	3/3	3/3	3/3	3/3	3/3	0/3
Iritis	3/3	3/3	3/3	3/3	2/3	1/3	1/3	0/3
*Conjunctivae:								
*Redness	3/3	3/3	3/3	3/3	3/3	0/3	0/3	0/3
*Chemosis	3/3	2/3	2/3	1/3	0/3	0/3	0/3	0/3
*Discharge	3/3	3/3	3/3	3/3	2/3	0/3	0/3	0/3

*Score of 2 or more required to be considered "positive."

A. Observations - All eyes exhibited corneal opacity, iritis and conjunctivitis from the one hour observation through 72 hours. No positive scores were noted for conjunctivitis on day 7. Corneal opacity and iritis resolved by day 14 when all eyes were free of irritation.

B. Reviewer's Conclusions: We agree with the study author that Phyton-016-B is moderately irritating to the eye.

Reviewer: Eugenia McAndrew **Date:** February 6, 2007
Risk Manager: 22

STUDY TYPE: Primary Dermal Irritation - Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid; pH 4.5)

CITATION: Durando, J. Phyton -016-B. Primary Skin Irritation Study in Rabbits. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 18080. October 4, 2005. MRID 46928507 Unpublished.

SPONSOR: Phyton Corporation, 7449 Cahill Road, Edina, MN 55439

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46928507), three young adult New Zealand albino rabbits (1 male and 2 female; Source: Robinson Services, Clemmons, NC) were dermally exposed to Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid). Five-tenths of a milliliter of the test substance was applied to one 6 cm^2 intact dose site on each animal for a period of four hours. Test sites were covered with a gauze pad and wrapped with semi-occlusive tape. Animals were then observed at 1, 24, 48 and 72 hours after patch removal. Irritation was scored by the method of Draize.

Primary Dermal Irritation Index (PDII) = 1.5 One hour after patch removal, all sites exhibited well defined erythema and very slight edema. The irritation decreased with time. All sites were free of irritation by 72 hours.

In this study, the formulation is slightly irritating. EPA Toxicity Category IV.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

INDIVIDUAL SKIN IRRITATION

ERYTHEMA/EDEMA

Animal No.	Sex	Hours After Patch Removal			
		1	24	48	72
15080	F	2/1	1/1	1/0	0/0
15081	M	2/1	1/1	1/0	0/0
15082	F	2/1	1/1	1/0	0/0

A. Observations - One hour after patch removal, all sites exhibited well defined erythema and very slight edema. The irritation decreased with time. All sites were free of irritation by 72 hours.

B. Results - Primary Dermal Irritation Index (PDII) = 1.5

C. Reviewer's Conclusions - We agree with the study author that Phyton-016-B is slightly irritating to the skin.

Reviewer: Eugenia McAndrew **Date:** February 6, 2007
Risk Manager: 22

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid)

CITATION: Moore, G. Phyton -016-B. Dermal Sensitization Study in Guinea Pigs (Buehler Method). Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 18397. March 2, 2006. MRID 46928508 Unpublished.

SPONSOR: Phyton Corporation, 7449 Cahill Road, Edina, MN 55439

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46928508) with Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid),30 Hartley albino male guinea pigs (Source: Elm Hill Breeding Labs, Chelmsford, MA; 345-423 g) were tested using the Buehler method. The procedures were validated using alpha-Hexylcinnamaldehyde (HCA) as the positive control substance in PSL Study #18271.

Once each week for three weeks, 0.4 mL of a 12% w/w mixture of the test substance in distilled water was applied to the left side of 20 test animals for a 6-hour exposure period for a total of three exposures. Readings were made 24 and 48 hours after each induction application. The animals were left untreated for two weeks. For the challenge 27 days after the first induction, 0.4 mL of a 3% w/w mixture of the test substance in distilled water (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Ten naive control guinea pigs were treated with the 3% w/w mixture of the test substance in distilled water at challenge only. Readings were made at 24 and 48 hours after the exposure period.

In this study, the formulation is not a dermal sensitizer**.**

Very faint to well defined erythema (0.5-1) was noted at all test animal sites during the induction phase. Following the challenge, very faint erythema (0.5) was observed at 7/20 test animal sites at 24 hours only. In the naive control group, very faint erythema (0.5) was noted at 5/10 sites at 24 hours. No positive responses were noted in either the test or naïve control animals.

This study is classified as Acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. PROCEDURE

A. Induction - Once each week for three weeks, 0.4 mL of a 12% w/w mixture of the test substance in distilled water was applied to the back of each test animal for a 6-hour exposure period for a total of three exposures. Readings were made at 24 and 48 hours after the exposure periods.

B. Challenge - Twenty-seven days after the first induction dose, 0.4 mL of a 3% w/w mixture of the test substance in distilled water (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Readings were made at 24 and 48 hours after the exposure period.

C. Naive Controls - Ten naive control guinea pigs were treated with the 3% w/w mixture of the test substance in distilled water at challenge only.

II. RESULTS and DISCUSSION:

A. Reactions and duration - Very faint to well defined erythema (0.5-1) was noted at all test animal sites during the induction phase. Following the challenge, very faint erythema (0.5) was observed at 7/20 test animal sites at 24 hours only. In the naive control group, very faint erythema (0.5) was noted at 5/10 sites at 24 hours. No positive responses were noted in either the test or naïve control animals.

B. Positive control - The positive results of the HCA study # 18271 validates the test system used in this study.

C. Reviewer's Conclusions: We agree with the study author that based on the findings and evaluation system used, Phyton-016-B is not considered to be a contact sensitizer.

ACUTE TOX ONE-LINERS

1. DP BARCODE: D332607
2. PC CODE: 024401
3. CURRENT DATE: 06/FEB/2007
4. TEST MATERIAL: Phyton-016-B (Lot # 6887; 21.3% copper sulfate pentahydrate; greenish dark gray liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity / rat Product Safety Lab 18394/3-2-06	46928503	LD_{50} = 1030 mg/kg (females)	III	A
Acute dermal toxicity / rat Product Safety Lab 18395/3-2-06	46928504	LD_{50} > 5000 mg/kg (males and females)	IV	A
Acute inhalation toxicity / rat Product Safety Lab 18396/3-2-06	46928505	LC_{50} > 2.06 mg/L (males and females)	IV	A
Primary eye irritation / rabbit Product Safety Lab 18079/10-4-05	46928506	Corneal opacity, iritis and conjunctivitis in 3/3 eyes from one hour through 72 hours. All eyes free of irritation by day 14.	II	A
Primary dermal irritation / rabbit Product Safety Lab 18380/10-4-05	46928507	PDII = 1.5 Well defined erythema and very slight edema at 3/3 sites at one hour. All sites free of irritation by 72 hours.	IV	A
Dermal sensitization / guinea pig Product Safety Lab 18397/3-2-06	46928508	Not a sensitizer	--	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived